

PATENT
Attorney Docket No. **DHI-06207**

REMARKS

1. Summary of Interview

A telephone interview on 12/17/03 was attended by the inventor, Dr. Yung Huang, Dr. David Scholl who is an expert in molecular virology, the undersigned Applicant's representative, Dr. Maha Hamdan, and the PTO's representatives, Examiner Shannon Foley and Primary Examiner James Housel.

The non-obviousness of the pending claims was discussed, and Dr. Huang advanced his factually based opinion of non-obviousness of the claims in view of his data with different cell lines. The Examiner and Primary Examiner indicated that the claims would be allowable if Dr. Huang's opinion was submitted in the form of a Declaration. Accordingly, a Declaration by Dr. Huang is enclosed.

2. Restriction Requirement

Claims 1-14 and 19-51 are pending.

The Examiner withdrew Claims 19-51 "from consideration as being directed to a non-elected invention."¹ Claim 19-51 have been cancelled. Applicant's cancellation of the claims does not narrow the scope of any of the claims within the meaning of *Festo*,² because cancellation of non-elected claims is not related to a statutory requirements for a patent, but rather is related to the Patent Office's convenience for organizing searches. Claim cancellations were made notwithstanding Applicant's belief that the cancelled claims would have been allowable, without acquiescing to any of the Examiner's arguments, and without waiving the right to prosecute the cancelled (or similar) claims in another application, but rather for the purpose of furthering Applicant's business goals and expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG).³

1 Paper No. 17, page 3, first paragraph.

2 *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, U.S., No. 00-1543, 5/28/02.

3 65 Fed. Reg. 54603 (September 8, 2000).

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3. Withdrawn Rejection

Applicant notes, with appreciation, that the Examiner withdrew the rejection of Claims 1-3, 6, 7, and 11-14 under 35 U.S.C. §112, first paragraph, for alleged lack of enablement, since this rejection has not been maintained in the instant Office Action.

4. Response to Rejection of The Claims

A. Claims 1-4 and 6-14 are non-obvious over Scholl *et al.* and Powell *et al.*

Claims 1-4 and 6-14 were rejected under 35 U.S.C. §103(a) as being allegedly obvious over Scholl *et al.*⁴ and Powell *et al.*^{5,6} Applicant respectfully must traverse because a *prima facie* case of obviousness, if arguably made, is rebutted by Dr. Huang's Declaration and the following remarks.

As explained by Dr. Huang's Declaration (item 2 (i)), the Examiner erroneously assumed that "a recombinant DAF receptor would only increase susceptibility in a cell that is already susceptible to enterovirus infection." Furthermore, the references do not provide a reasonable expectation of success that increasing the number of copies of DAF in a cell that is already susceptible to enterovirus would increase sensitivity to the enterovirus (Declaration, item 2(ii)).

In addition, the Examiner did not explain why Applicant's failure to increase susceptibility of the H292 cells by transfection with hDAF should be ignored, while a success in increasing susceptibility of BGМК cells by transfection with hDAF should allegedly be expected.

Furthermore, nothing in the cited references teaches one of ordinary skill in the art whether or not the sensitivity of wild type BGМК to enterovirus is exhausted and/or saturated similarly to H292. Therefore, one of ordinary skill in the art they would have no scientific basis to reasonably predict whether or not the sensitivity of BGМК cells to enteroviruses

4 US patent 6,168,915.

5 Powell *et al.* (1998) J. Gen. Virol. 79:1707-1713.

6 Paper No. 17, middle of page 3.

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could be increased. Rather, this result would have had to be determined **empirically**, as done by Applicant.

Applicant previously submitted Harrington *et al.*⁷ and Chesebro *et al.*⁸ in support of their position that the prior art rebuts any alleged reasonable expectation of success by demonstrating that expression of a virus receptor by a cell is **not** sufficient for binding of the virus to the cell and/or for permissiveness of the cell to the virus. The Examiner responded that "...the art cited by applicant is not analogous to the instant invention. HIV and Enterovirus have different modes of replication, infection, etiology and pathology."⁹

However, the examiner improperly applies a narrow definition of analogous art. Under the law, "[t]he determination that a reference is from a nonanalogous art is therefore two fold. First, we decide if the reference is within the field of the inventor's endeavor. If it is not, we proceed to determine whether the reference is reasonably pertinent to the particular problem with which the inventor was involved."¹⁰ Here, Harrington's and Chesebro's work relates to the **same field of endeavor** as the inventor's work, i.e., determining whether there is one or more factor that is involved in virus entry into a cell, and thereby determining the cell's susceptibility. Additionally, Harrington's and Chesebro's work addresses the **same problem**, i.e., whether expression of one receptor is sufficient to increase entry of a virus into a cell. Since Harrington's and Chesebro's work is not only in the same field of endeavor, but also addresses the same problem as in the invention, these references are analogous art.

Furthermore, both of the Harrington and Chesebro references (like Powell *et al.* that was cited by the Examiner) show that susceptibility to a virus may be mediated by more than one receptor, and that transfection of cells with one receptor does not necessarily increase

7 Harrington *et al.* (1993) J. Virology 67(10):5939-5947.

8 Chesebro *et al.* (1990) J. Virology 64(1):215-221.

9 Paper No. 17, page 5, last paragraph.

10 *In re Wood*, 599 F.2d 1032, 1036, 202 USPQ 171, 174 (CCPA 1979); *In re Octiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992).

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sensitivity of the trasfected cells to the virus.¹¹ Based on this teaching, in addition to Powell's teaching that enterovirus "interact with more than one cellular receptor,"¹² one of ordinary skill in the art would have no scientific basis for predicting whether or not expression of the single receptor DAF would increase sensitivity of BGMK cells to enterovirus infection.

Rather, this result has to be determined **empirically**, as done by Applicant.

Moreover, the Examiner inaccurately stated that Harrington and Chesebro "discuss HIV infection in cells that are **not** normally susceptible to HIV infection."¹³ However, the cells used by the references are susceptible to HIV. For example, Chesebro shows that "even in the absence of CD4 expression **all** three cell types [i.e., HeLa, astrogloma, and squamous cell carcinoma cells] showed low but **significant levels of infection** by most HIV strains."¹⁴

In view of the above and of Dr. Huang's Declaration, withdrawal of the rejection of Claims 1-4 and 6-14 under 35 U.S.C. §103(a) over Scholl *et al.* and Powell *et al.* is respectfully requested.

B. Claim 5 is non-obvious over Scholl *et al.*, Powell *et al.*, Spiller *et al.*, GenEmbl accession no. M15799, and GenEmbl accession no. M30142

Claim 5 was rejected under 35 U.S.C. §103(a) for alleged obviousness over Scholl *et al.*, Powell *et al.*, Spiller *et al.*¹⁵, and either the sequence alignment of SEQ ID NO:1 with

11 For example, Chesebro shows "the existence of HIV receptor mechanism unrelated to CD4..." (Chesebro *et al.*, page 220, column 1, last sentence). Thus, Chesebro shows that susceptibility to a virus may be mediated by more than one receptor. Also, Chesebro shows that different strains of the same virus use different cell receptors. For example, Chesebro shows that different HIV strains "use either CD4 or non-CD4 receptors on different cell types" For example, the CD-4 positive U87MG cells were highly infected by the HIV strain NY5 but not by the IIIB strain (Chesebro *et al.*, page 220, column 1, first full paragraph). This shows that cell surface receptors are not the only molecules required for successful virus entry into, and infection of, cells.

12 Powell *et al.*, page 1707, Abstact, last sentence.

13 (Emphasis added) Paper No. 17, page 5, last paragraph.

14 (Emphasis added) Chesebro *et al.*, page 215, column 1, third paragraph.

15 Spiller *et al.* (2000) J. Infectious Diseases 181:340-343.

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GenEmbl accession no. M15799 of Medoff *et al.*,¹⁶ or the sequence alignment of SEQ ID NO:3 with GenEmbl accession no. M30142 of Caras *et al.*^{17,18} on the ground that "there is no deficiency to remedy" by the sequence alignments.¹⁹ Applicant respectfully must disagree.

Applicant incorporates Dr. Huang's Declaration item 3(i), the above arguments, as well as Applicant's prior arguments that the primary Scholl *et al.* reference and secondary Powell *et al.* reference are deficient because (a) Powell *et al.*'s success was **limited to the mouse WOP cells** that were transfected with decay accelerating factor (DAF), (b) Powell *et al.* **teaches away** from the invention by teaching that CHO cells and RD cells that express decay accelerating factor do not bind to, nor are permissive for, enteroviruses, and (c) Powell *et al.* **teaches away** from the invention by teaching that enterovirus binding to cells, and the cells' permissiveness for enteroviruses is **not necessarily** mediated by binding of the enterovirus to decay accelerating factor, but is rather mediated via **alternative unidentified receptor(s)**. Thus, motivation to combine the references to arrive at the claimed compositions is lacking.

Referring to the alleged "reasonable expectation of success" in arriving at the claimed combination, Applicant incorporates Dr. Huang's Declaration item 3(ii), the above arguments, as well as Applicant's prior arguments that the additionally cited Spiller *et al.* and sequence alignments do **not** bridge the following gaps in the disclosure of Scholl *et al.* and Powell *et al.* references: a) Scholl *et al.*'s **silence** and Powell *et al.*'s reported **failure** in two cell types (*i.e.*, CHO cells and RD cells) to bring about either binding of enterovirus to a cell expressing DAF, or permissiveness of such a cell to enteroviruses, (b) Applicant's data showing that H292 cells that are transfected with hDAF do **not** show increased sensitivity to enteroviruses, and c) Harrington *et al.* and Chesebro *et al.* that demonstrate that expression of a virus receptor by a cell is **not** sufficient for binding of the virus to the cell and/or for permissiveness of the cell to the virus.

16 Medoff *et al.* (1987) PNAS 84(7):2007-2011.

17 Caras *et al.* (1987) Nature 325-(6104):545-549.

18 Paper No. 17, paragraph bridging pages 6 and 7.

19 Paper No. 17, page 7, first full paragraph.

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Applicant therefore respectfully requests withdrawal of the rejection of Claim 5 for alleged obviousness under 35 U.S.C. §103(a) over Scholl *et al.*, Powell *et al.*, Spiller *et al.*, and either the sequence alignment of SEQ ID NO:1 with GenEmbl accession no. M15799 of Medoff *et al.*, or the sequence alignment of SEQ ID NO:3 with GenEmbl accession M30142 of Caras *et al.*

CONCLUSION

All grounds of rejection and objection of the Office Action of November 5, 2003 having been addressed, reconsideration of the application is respectfully requested. Applicant respectfully requests the Examiner to call the undersigned before drafting another written communication, if any.

Dated: March 2, 2004

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